UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/527,665 | 03/11/2005 | Christophe de Romeuf | 065691-0388 | 7255 |

22428 7590 08/06/2008
FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

| EXAMINER | |
|---|---|
| DAHLE, CHUN WU | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 08/06/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/527,665 | DE ROMEUF ET AL. | |
| | Examiner | Art Unit | |
| | CHUN DAHLE | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *37 and 38* is/are pending in the application.

4a) Of the above claim(s) *37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 6, 2008, has been entered.

2. Applicant's amendment to the claims, filed on November 28, 2007, has been entered.

Claims 1-37 have been canceled.
Claims 37 and 38 are pending.

Claim 37 has been withdrawn from further consideration under 37 C.F.R. 1.142(b) as being drawn to nonelected invention.

Claim 38 is currently under consideration.

3. This Office Action will be in response to applicant's arguments, filed on November 28, 2007.

4. Applicant's request for reconsideration of petition under 37 C.F.R. 1.48(a), to add two new joint inventors Nicolas Bihoreau and Emmanuel Nony and to correct spelling error of previous listed inventor Arnaud Clacet to Arnaud Glacet, has been entered. A new BIB Sheet reflecting the corrected inventorship is attached herein.

5. In view of applicant's amendment to the claim, the prior rejections under 35 U.S.C. 112, second paragraph have been withdrawn.

6. In view of applicant's amendment to the claim, the prior rejection under 35 U.S.C. 112, first paragraph, enablement, has been withdrawn.

7. In view of applicant's amendment to the claim, the prior rejection under 35 U.S.C. 112, first paragraph, written description, new matter, has been withdrawn.

8. In view of applicant's amendment to the claim, the prior rejection under 35 U.S.C. 102(b), has been withdrawn.

9. Claim 38 is objected to for following informalities:

Claims 38 recites "bringing a CD16-transformed effector cell Jurkat CD16, into a reaction medium with the monoclaonal antibody…". Applicant is required to clarify this limitation.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The purpose of the selection of monoclonal antibody is not defined. Claim 38 recites "A method for selecting monoclonal antibody" and "selecting an antibody for which the level of said IL-2 release is increased by more than 100% compared with a negative control…", yet the purpose of selection method is unclear and ambiguous.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 38 is drawn to a method for selecting a monoclonal antibody, wherein the method comprises following steps:

a) bringing a CD16-transformed Jurkat cell into a reaction medium with the monoclonal antibody and the antigen for said antibody,

b) measuring the amount of IL-2 cytokine released, and

c) selecting an antibody for which the level of said IL-2 release is increased by more than 100% compared with a negative control.

The instant specification discloses antibodies made in host cells such as YB2/0 exhibit enhanced ADCC. The instant specification further discloses methods of measuring Fc-related functions of antibodies, e.g. anti-Rh(D) antibody, by measuring effector cell activation using assays including ADCC and cytokine releases from Jurkat/CD16 cells (see page 4-5, in particular). Furthermore, the specification discloses that the amount of IL-2 released by the Jurkat/CD16 cells correlates positively with ADCC mediated through effector cells (e.g. see pages 14-16).

However, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate

in scope with the claim. The instant specification does not provide sufficient enabling description of the claimed method for selecting a monoclonal antibody by using CD16 expressing Jurkat cells, performing an ADCC assay and measuring the amount of IL-2, wherein the amount of IL-2 correlates with ADCC. The instant specification appears to only disclose methods of evaluating the effector function ADCC that is related to the Fc region of an antibody.

The instant claim encompasses in its scope any and all monoclonal antibodies including those that have antigen specificities against cell surface molecules on Jurkat cells. However, the claimed method is based on interaction of Fc region of an antibody and CD16 receptor on Jurkat cells and the method correlates the secretion of IL-2 by Jurkat/CD16 cells and the CD16 mediated ADCC function (e.g. see Figure 4 of the instant specification). Therefore, it is not clear antibodies that would have antigen specificities to Jurkat/CD16 cell surface molecules, such as anti-CD16 antibody or anti-CD3 antibody, would be applicable to the claimed methods since those antibodies interact with Jurkat/CD16 via antigen binding region of the antibodies.

For example, the instant specification clearly shows that anti-CD16 antibody 3G8 inhibits ADCC function (e.g. see Figure 3 and page 11 of the instant specification). It is not clear how monoclonal anti-CD16 antibody can be selected by the claimed method by correlating IL-2 production and ADCC. In addition, Vivier et al. (International Immunity 1992, 4;11:1313-1323, reference on PTO-892 mailed on November 30, 2005) teach that Jurkat cells over-expressing CD16 loss CD3:TCR on the cell surface, resulting in the lost of IL-2 production upon stimulation of anti-CD3 antibody (e.g. see right column on page 1321). Thus, the claimed method would not be able to select anti-CD3 antibody based on correlating IL-2 release and ADCC function.

Further, the claim encompasses a method for selecting monoclonal antibody following the recited steps but it is not clear what the monoclonal antibody is selected for. Therefore, one of skill in the art would not be able to make and use the claimed method for selecting antibody for unknown purposes.

In view of the quantity of experimentation necessary, the limited working example, the

unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

14. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a *Written Description*, New Matter rejection.

The phrase "wherein the measurement of the amount of IL-2 is linearly correlated to the CD16 specific ADCC activity" as recited in claim 38 is not supported by the original disclosure or claim as filed.

Applicant's amendment, filed November 28, 2007, directs to support to Figure 10, pages 13 and 16 of the instant specification, and asserts that no new matter has been added.

However, the specification as filed does not provide sufficient written description of the above-mentioned "limitation". The specification does not provide sufficient support for linear correlation between CD16-specific activity and the amount of IL-2 released. The specification only discloses anti-D antibody induces ADCC correlates linearly with IL-2 release from Jurkat/CD16 cells; the instant claim now recites a method of selecting any and all monoclonal antibodies "wherein the measurement of the amount of IL-2 is linearly correlated to the CD16 specific ADCC activity", which were not clearly disclosed in the specification. Therefore, the claim represents a departure from the specification and claims originally filed. Applicant's reliance on a single species does not provide sufficient direction and guidance to the features currently claimed (any and all monoclonal antibodies).

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of

35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Eileen O'Hara can be reached 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chun Dahle/
Primary Examiner, Art Unit 1644

Chun Dahle, Ph.D. (formerly Chun Crowder)
Patent Examiner
July 31, 2008